





IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Re Application of: Kenneth J. Rothschild *et al.*

Serial No.: 10/719,523

Filed: 11/21/03

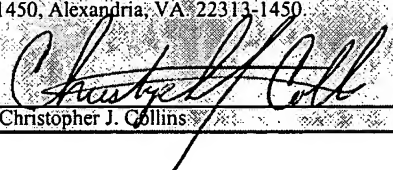
Entitled: **Methods For The Detection, Analysis And  
Isolation Of Nascent Proteins**

Group No.: 1636

Examiner: Schlapkohl, W.

**INFORMATION DISCLOSURE STATEMENT**

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA. 22313-1450

<b>CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)</b>	
I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.	
Dated: <u>August 21, 2006</u>	By:  Christopher J. Collins

Sir or Madam:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following printed publications are referred to in the body of the specification:

- U.S. Pat. No. 4,683,195 to Mullis *et al.*;
- U.S. Pat. No. 4,774,339 to Haugland *et al.*;
- U.S. Pat. No. 5,069,769 to Fujimiya *et al.*;
- U.S. Pat. No. 5,091,328 to Miller;
- U.S. Pat. No. 5,137,609 to Manian *et al.*;
- U.S. Pat. No. 5,187,288 to Kang *et al.*;
- U.S. Pat. No. 5,190,632 to Fujimiya *et al.*;
- U.S. Pat. No. 5,248,782 to Haugland *et al.*;
- U.S. Pat. No. 5,274,113 to Kang *et al.*;
- U.S. Pat. No. 5,433,896 to Kang *et al.*;
- U.S. Pat. No. 5,451,663 to Kang *et al.*;
- U.S. Pat. No. 5,643,722 to Rothschild *et al.*;

- U.S. Pat. No. 5,654,150 to King *et al.*;
- U.S. Pat. No. 5,783,397 to Hughes *et al.*;
- PCT WO90/05785 to Schultz;
- Allen *et al.*, *Gel Electrophoresis and Isoelectric Focusing of Proteins*, Walter de Gruyter, New York 1984, pp.17-62;
- *Antibodies: A Laboratory Manual* (E. Harlow and D. Lane, editors, Cold Spring Harbor Laboratory Press, 1988) pp.53,72-73;
- Bain *et al.*, "Site-Specific Incorporation of Nonnatural Residues during In Vitro Protein Biosynthesis with Semisynthetic Aminoacyl-tRNAs," *Biochemistry* 30:5411-21 (1991);
- Bruce and Uhlenbeck, "Specific Interaction of Anticodon Loop Residues with Yeast Phenylalanyl-tRNA Synthetase," *Biochemistry* 21:3921-3926 (1982);
- *Current Protocols in Molecular Biology* (F.M. Ausubel et al. editors, Wiley Interscience, 1993), 10-16,10-77;
- Da Poian, A. T., *et al.*, "Kinetics of intracellular viral disassembly and processing probed by Bodily fluorescence dequenching," *J Virol Methods* 70(1), 45-58 (1998);
- Doty *et al.*, "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemicals Studies," *Proc. Natl. Acad. Sci. USA* 46:461 (1960);
- DiCesare *et al.*, "A High-Sensitivity Electrochemiluminescence-Based Detection System for Automated PCR Product Quantitation," *BioTechniques* 15:152-59 (1993);
- Felgner *et al.*, "Lipofection: A highly efficient, lipid-mediated DNA-transfection procedure," *Proc. Natl. Acad. Sci. USA* 84:7413-17 (1987);
- Happ *et al.*, "New Approach to the Synthesis of 2'(3')-O-Aminoacyl Oligoribonucleotides," *J. Org. Chem.* 52:5387-91 (1987);
- Heckler *et al.*, "Preparation of 2'(3')-O-Acyl-pCpA Derivatives as Substrates for T4 RNA Ligase-Mediated "Chemical Aminoacylation"," *Tetrahedron* 40:87-94 (1984);
- Heckler *et al.*, "T4 RNA Ligase Mediated Preparation of Novel "Chemically Misacylated" tRNA<sup>Phe</sup>," *Biochemistry* 23:1468-73 (1984);
- Hemmila, I.A., Chemical Analysis "Applications of Fluorescence in Immunoassays", (Wiley&Sons 1991) pp.138-159;
- Hudson, "Methodological Implications of Simultaneous Solid-Phases Peptide Synthesis. 1. Comparison of Different Coupling Procedures," *J. Org. Chem.* 53:617-624 (1988);

- Krieg *et al.*, "Photocrosslinking of the signal sequence of nascent preprolactin to the 54-kilodalton polypeptide of the signal recognition particle," *Proc. Natl. Acad. Sci. USA* 83:8604-08 (1986);
- Keller, R. C., *et al.*, "Characterization of the Resonance Energy Transfer Couple Coumarin-Bodily and its Possible Applications in Protein-Lipid Research," *Biochem Biophys Res Commun* 207(2), 508-14 (1995);
- Kim, D., and Choi, C., "A Semicontinuous Prokaryotic Coupled Transcription/Translation System Using a Dialysis Membrane," *Biotechnol Prog* 12, 645-649 (1996) ;
- Kopp *et al.*, "Chemical Amplification: Continuous Flow PCR on a Chip," *Science* 280:1046 (1998);
- Kozak, "Point Mutations Define a Sequence Flanking the AUG Initiator Codon that Modulates Translation by Eukaryotic Ribosomes," *Cell* 44:283-292 (1986);
- Kudlicki, W.*et al.*, "Chaperone-dependent Folding and Activation of Ribosome-bound Nascent Rhodanese," *J Mol Biol* 244(3), 319-31 (1994);
- Laemmli, U. K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophage T4," *Nature* 227:680-685 (1970);
- Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Biological Studies," *Proc. Natl. Acad. Sci. USA* 46:453-461 (1960);
- *Molecular Cell Biology* (J. Darnell *et al.* editors, Scientific American Books, N.Y., N.Y. 1991) pp.119-132;
- Neu and Heppel, "Nucleotide Sequence Analysis of Polyribonucleotide by Means of Periodate Oxidation Followed by Cleavage with an Amine," *J. Biol. Chem.* 239:2927-34 (1964);
- Noren *et al.*, "A General Method for Site-Specific Incorporation of Unnatural Amino Acids into Proteins," *Science* 244:182-188 (1989);
- Odom, O. W., *et al.*, "In vitro engineering using acyl-derivatized tRNA," In *Protein synthesis: Methods and Protocols*, PP.93-103, (Humana Press, Totowa, NJ.);
- Patchornik *et al.*, "Photosensitive Protecting Groups," *J. Am. Chem. Soc.* 92:6333-35 (1970);
- Pavlopoulos, *et al.*, "Laser action from a tetramethylpyrromethene-BF.sub.2 complex," *APP. OPTICS* 27:4998-4999 (1988);

- Pfahler *et al.*, Sensors and Actuators, A21-A23 , pp. 431-434 (1990)<sup>1</sup>;
- Pillai, "Photoremovable Protecting Groups in Organic Synthesis," *Synthesis* 1-26 (1980);
- Powell *et al.*, "Molecular Diagnosis of Familial Adenomatous Polyposis," *N. Engl. J. Med.* 329:1982-87 (1993);
- Pratt, "Coupled Transcription-Translation in Prokaryotic Cell-Free System," (*Transcription and Translation*, B.D. Hames and S.J. Higgins, Editors, p. 179-209, IRL Press, Oxford, 1984);
- Promega Technical Bulletin No. 182; tRNA<sup>nscend</sup><sup>TM</sup>: Non-radioactive Translation Detection System, Sept. 1993;
- Reis, R. C., *et al.*, "A novel methodology for the investigation of intracellular proteolytic processing in intact cells," *Eur J Cell Biol* 75(2), 192-7 (1998);
- Rowan and Bodmer, "Introduction of a *myc* Reporter Taq to Improve the Quality of Mutation Detection Using the Protein Truncation Test," *Human Mutation* 9:172-176 (1997);
- Sampson and Uhlenbeck, "Biochemical and physical characterization of an unmodified yeast phenylalanine transfer RNA transcribed *in vitro*," *Proc. Natl. Acad. Sci. USA* 85:1033-37 (1988);
- Seong and RajBhandary, "*Escherichia coli* formylmethionine tRNA: Mutations in GGG sequence conserved in anticodon stem of initiator tRNAs affect initiation of protein synthesis and conformation of anticodon loop," *Proc. Natl. Acad. Sci. USA* 84:334-338 (1987);
- Spirin *et al.*, "A Continuous Cell-Free Translation System Capable of Producing Polypeptides in High Yield," *Sci.* 242:1162-64 (1988);
- Stephen, "High-Resolution Preparative SDS-Polyacrylamide Gel Electrophoresis: Fluorescent Visualization and Electrophoretic Elution-Concentration of Protein Bands," *Anal. Biochem.* 65:369-79 (1975);
- Treibs & Kreuzer, "Difluoroboryl-komplexe von di- und tripyrrylmethenen," *Liebigs Ann. Chem.* 718:208-223 (1968);
- Turcatti *et al.*, "Probing the Structure and Function of the Tachykinin Neurokinin-2 Receptor through Biosynthetic Incorporation of Fluorescent Amino Acids at Specific Sites," *J Biol Chem* 271(33), 19991-8 (1996);

---

<sup>1</sup> We have been unable to obtain this reference, but if the examiner requests a copy we will again seek to obtain it.

- Van Lintel *et al.*, *Sensors and Actuators* 15:153-167 (1988)<sup>2</sup>;
- Varshney U. and RajBhandary UL, "Initiation of protein synthesis from a termination codon," *Proc Natl Acad Sci U S A* 87(4):1586-90 (1990);
- Varshney *et al.*, "Direct Analysis of Aminoacylation Levels of tRNA<sup>a</sup> in Vivo," *J. Biol. Chem.* 266: 24712-24718 (1991);
- Yao S *et al.*, "SDS capillary gel electrophoresis of proteins in microfabricated channels," *PNAS* 96:5372-5377 (1999);
- Vecesey-Semjen *et al.*, "The Staphylococcal  $\alpha$ -Toxin Pore Has a Flexible Conformation," *Biochemistry* 38 4296-4302 (1999);
- Vos de Waal *et al.* (1977)<sup>3</sup>;
- Walker, B. *et al.*, "Functional Expression of the  $\alpha$ -Hemolysin of *Staphylococcus aureus* in Intact *Escherichia coli* and in Cell Lysates," *J. Biol. Chem.* 267:10902-10909 (1992); and
- Worries *et al.*, "A novel water-soluble fluorescent probe: Synthesis, luminescence and biological properties of the sodium salt of the 4-sulfonato-3,3', 5'-tetramethyl-2,2'-pyrromethen-1,1'-BF<sub>3</sub> complex," *Recl. Trav. Chim. PAYSBAS* 104, 288 (1985)<sup>4</sup>;

Applicants have become aware of the following printed publications which may be material to the examination of this application:

- U.S. Pat. No. 4,675,285 to Clark *et al.*, provides a method for identification of clones expressing the desired protein from the cDNA libraries
- U.S. Pat. No. 5,709,998 to Kinzler *et al.*, describes APC gene, its mutations and mutations linked condition (familial adenomatous polyposis, FAP). Primers, and method for mutation detection using protein truncation test with radioactive readout is also provided.
- U.S. Pat. No. 5,861,494 to Soppet *et al.*, describes APC gene, its mutations and mutations linked condition (familial adenomatous polyposis, FAP). Primers, and method for mutation detection using protein truncation test with radioactive readout is also provided.

---

<sup>2</sup> We have been unable to obtain this reference, but if the examiner requests a copy we will again seek to obtain it.

<sup>3</sup> We have been unable to obtain this reference, but if the examiner requests a copy we will again seek to obtain it.

<sup>4</sup> We have been unable to obtain this reference, but if the examiner requests a copy we will again seek to obtain it.

- U.S. Pat. No. 5,622,829 to King *et al.*, disclose the sequences of breast and ovarian cancer susceptibility genes (BRCA1). Hybridization-based methods are also described for the detection of specific mutations.
- U.S. Pat. No. 5,693,473 to Shattuck-Eidens *et al.* disclose the sequences of breast and ovarian cancer susceptibility genes (BRCA1). Hybridization-based methods are also described for the detection of specific mutations.
- U.S. Pat. No. 5,760,207 to Kinzler *et al.*, describes APC gene, its mutations and mutations linked condition (familial adenomatous polyposis, FAP). Primers, and method for mutation detection using protein truncation test with radioactive readout is also provided.
- U.S. Pat. No. 5,879,890 to Laken *et al.*, describes APC gene, its mutations and mutations linked condition (familial adenomatous polyposis, FAP). Primers, and method for mutation detection using protein truncation test with radioactive readout is also provided.
- Czworkowski *et al.*, "Fluorescence Study of the Topology of Messenger RNA Bound to the 30S Ribosomal Subunit of *Escherichia coli*," *Biochemistry* 30:4821-4830 (1991), describes the interaction of fluorescently labeled RNAs (25-36 nucleotides in length) with the fluorescently labeled 30S subunit of *Escherichia coli* studied by using fluorescence spectroscopic techniques.
- Hardesty *et al.*, "Ribosome function determined by fluorescence," *Biochimie* 74:391-401 (1992). This paper is a review on ribosome function.
- Picking *et al.*, "The use of synthetic tRNA as probes for examining nascent peptides on *Escherichia coli* ribosomes," *Biochimie* 73:1101-1107 (1991), the cell free synthesis of N-acetyl or N-acyl coumarin labeled polycysteine and polyserine were carried out on *Escherichia coli* ribosomes using N-acyl coumarin derivatives of either Ser-tRNA or Phe-tRNA. The properties of the resulting nascent peptides were studied by fluorescence spectroscopy and compared to those of nascent polyphenylalanine chains synthesized under similar conditions.
- Picking *et al.*, "Evidence for RNA in the Peptidyl Transferase Center of *Escherichia coli* Ribosomes as Indicated by Fluorescence," *Biochemistry* 31:12565-12570 (1992), The interaction of coumarin labeled (tRNA(phe)) [either the amino acid or the 5' end] with ribosomes was studied using fluorescence spectroscopy.
- Picking *et al.*, "The Conformation of Nascent Polylysine and Polyphenylalanine Peptides on Ribosomes," *J. of Biological Chemistry* 266:1534-1542 (1991),

describes the behavior of fluorescently labeled polylysine and polyphenylalanine during their in vitro synthesis on *E. coli* ribosomes.

- Picking *et al.*, "Fluorescence Characterization of the Environment Encountered by Nascent Polyalanine and Polyserine as They Exit *Escherichia coli* Ribosomes during Translation," *Biochemistry* 31:2368-2375 (1992), describes a coumarin probe placed at the alpha-amino group of a synthetic elongator alanyl-tRNA or a synthetic initiator alanyl-tRNA or at the epsilon-amino group of natural lysyl-tRNA, and each was used to nonenzymatically initiate peptide synthesis.
- Picking *et al.*, "A synthetic alanyl-initiator tRNA with initiator tRNA properties as determined by fluorescence measurements: Comparison to a synthetic alanyl-elongator tRNA," *Nucleic Acids Research* 19:5749-5754 (1991). A derivative of coumarin [3-(4-maleimidophenyl)-7-diethyl-amino-4-methylcoumarin] was covalently attached to the alpha amino group of alanine of the two synthetic Ala-tRNA species. The fluorescence spectra, quantum yield and anisotropy for the two Ala-tRNA derivatives were studied after they were bound to 70S ribosomes.
- Ma *et al.*, "In Vitro Protein Engineering Using Synthetic tRNA<sup>Ala</sup> with Different Anticodons," *Biochemistry* 32:7939-7945 (1993), describes the use of synthetic tRNA for in vitro protein engineering was tested in a coupled transcription/translation system prepared from *Escherichia coli*.
- Odom *et al.*, "Movement of tRNA but Not the Nascent Peptide during Peptide Bond Formation on Ribosomes," *Biochemistry* 29:10734-10744 (1990), The interaction of fluorescently [(3-(4-maleimidophenyl)-7-diethyl-amino-4-methylcoumarin) or (5-[[2-[(iodoacetyl)amino]ethyl]amino]naphthalene-1-sulphonic acid)] labeled (Phe) tRNA at the 5'-end with ribosome as well as with nascent polypeptide was investigated using nonradiative energy transfer.
- U.S. Patent No. 5,614,386 to Metzker *et al.*, describes dyes for use in labeling DNA primers for improved DNA sequencing techniques.
- European Pat. No. 0234799A2 to Kurzchalia *et al.*, describes methods for the detection and isolation of protein utilizing the incorporation of photoaffinity reagents and biotin or other haptens into nascent peptides.
- Crowley *et al.*, "The signal sequence moves through a ribosomal tunnel into a noncytoplasmic aqueous environment at the ER membrane early in translocation," *Cell* 73:1101-1115 (1993). This reference examines the logistics of nascent peptide production by utilizing eNBD-Lys-tRNA analogs to examine the environment of a nascent peptide chain as it moved through the ribosome and into the ER membrane.



- Karolin *et al.*, "Fluorescence and Absorption Spectroscopic Properties of Dipyrrometheneboron Difluoride (BODIPY) Derivatives in Liquids, Lipid Membranes, and Proteins," *J. Am. Chem. Soc.* 116:7801-7806 (1994) describes the use of a fluorescent dye, (BODIPY) to label a modified plasminogen activator inhibitor protein after the protein had been isolated.
- Hardesty *et al.*, "Extension and Folding of Nascent Peptides on Ribosomes." The Translational Apparatus, Nierhaus *et al.* ed: New York and London; Plenum Press. p.347-358 (1993) describes peptide folding experiments where amino-tRNAs were modified after aminoacylation.
- Johnson *et al.*, "Protein Synthesis and Secretion as seen by the Nascent Protein Chain," The Translational Apparatus, Nierhaus *et al.* ed: New York and London; Plenum Press. p. 359-370 (1993) discloses peptide synthesis experiments where Lys-tRNA was modified after aminoacylation.
- Shore *et al.*, "A Fluorescent Probe Capable of Incorporation into Nascent Polypeptide Chains," 1986 *Federation Proceedings* 45, 1566 Abstract, discloses the attachment of a fluorescent moiety (N<sup>6</sup>-fluoresceinthioacetyl) onto a tRNA aminoacylated with lysine wherein the lysine has been modified by reaction with N-bromoacetoxysuccinimide.
- Shore *et al.*, "Accessibility of AA-tRNA and Nascent Chain During Protein Synthesis," 1988 *FASEB Journal* 2, A1045 Abstract, discloses the attachment of a fluorescent moiety (N<sup>6</sup>-fluoresceinthioacetyl) onto a tRNA aminoacylated with lysine thereby producing N<sup>6</sup>-fluoresceinthioacetyl-lys-tRNA.
- Bain *et al.*, "Site-Specific Incorporation of Non-Natural Residues into Peptides: Effect of Residue Structure on Suppression and Translation Efficiencies," *Tetrahedron* 47:2389-2400 (1991), discloses methods for the production of a series of 12 semi-synthetic acylated suppressor tRNAs.
- Johnson *et al.*, "N-Acetyllysine Transfer Ribonucleic Acid: A Biologically Active Analogue of Aminoacyl Transfer Ribonucleic Acids," *Biochemistry* 15:569-575 (1976), discloses methods for the production of N<sup>6</sup>-Acetyl-Lys-tRNA.
- Johnson, "Chemically Modified Aminoacyl-tRNA as a Probe of Ribosome Structure: the Synthesis and in vitro Activity of  $\epsilon$ -N-acetyl-Lys-tRNA," 1973 Thesis Excerpts, University of Oregon, Eugene, Oregon, discloses several methods of producing fluorescently labeled (N-methylantranilic acid) Lys-tRNA.
- Shore, "The Use of Fluorescent-Labeled Amino Acids to Examine the Environment of Ribosome-Bound Nascent Polypeptide Chains," 1991 Dissertation, University of Oklahoma, Norman Oklahoma, discloses the synthesis

of fluorescent analogs of Lys-tRNA including N<sup>6</sup>-fluoresceinthioacetyl-Lys-tRNA and N<sup>6</sup>-6-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)aminohexanoyl-Lys-tRNA.

- Kramer *et al.*, "In Vitro engineering using synthtic tRNAs with altered anticodons including four-nucleotide anticodons," *Methods Mol Biol.* 77:105-16 (1998) discloses methods for the synthesis of tRNAs with altered anticodons.

Applicants have become aware of the following printed 1999 publications:

- Kramer *et al.*, "N-terminal and C-terminal modifications affect of in vitro synthesized proteins," *Int J Biochem Cell Biol.* 31:231-41 (1999) discloses the effect of certain N-terminal and C-terminal modifications on protein synthesis. This publication modifies a N-acly-Met-tRNA<sub>f</sub> with coumarin after acetylation.
- Tsalkova *et al.*, "The effect of a hydrophobic N-terminal probe on translational pausing of chloramphenicol acetyl transferase and rhodanese," *J Mol Biol.* 286:71-81 (1999) discloses the effect of hydrophobic residues at the N-terminus in regards to protein synthesis. N-acetyl-S-coumarin-Met-tRNA<sub>f</sub> was used to generate the hydrophobic residues.
- Nemoto *et al.*, "Fluorescence labeling of the C-terminus of proteins with a puromycin analogue in cell-free translation systems," *FEBS Letters.* 462:43-46 (1999) discloses a method using puromycin analogues with a fluorescent moiety to label the C-terminus of nascent peptides.

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: August 21, 2006



Peter G. Carroll  
Registration No. 32,837

MEDLEN & CARROLL, LLP  
101 Howard Street, Suite 350  
San Francisco, California 94105  
617/984-0616

FORM PTO-1449  
(Modified)U.S. Department of Commerce  
Patent and Trademark Office

Attorney Docket No.: AMBER-08501

Serial No.: 10/719,523

INFORMATION DISCLOSURE STATEMENT BY APPLICANT  
(Use Several Sheets If Necessary)Applicant: Kenneth J. Rothschild *et al.*

(37 CFR § 1.98(b))

Filing Date: 11/21/03

Group Art Unit: 1636

## U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	Serial / Patent Number	Issue Date	Applicant / Patentee	Class	Subclass	Filing Date
	1	4,675,285	6/23/87	Clark <i>et al.</i>	435	6	9/19/84
	2	4,683,195	7/28/87	Mullis <i>et al.</i>	435	6	2/07/86
	3	4,774,339	9/27/88	Haugland <i>et al.</i>	548	405	8/10/87
	4	5,069,769	12/03/91	Fujimiya <i>et al.</i>	204	182.8	6/06/90
	5	5,091,328	2/25/92	Miller	437	52	11/21/89
	6	5,137,609	8/11/92	Manian <i>et al.</i>	204	180.1	1/31/92
	7	5,187,288	2/16/93	Kang <i>et al.</i>	548	110	5/22/91
	8	5,190,632	3/02/93	Fujimiya <i>et al.</i>	204	299 R	3/20/92
	9	5,248,782	9/28/93	Haugland <i>et al.</i>	548	110	12/18/90
	10	5,274,113	12/28/93	Kang <i>et al.</i>	548	405	11/01/91
	11	5,433,896	7/18/95	Kang <i>et al.</i>	252	700	5/20/94
	12	5,451,663	9/19/95	Kang <i>et al.</i>	530	367	4/08/93
	13	5,614,386	3/25/97	Metzker <i>et al.</i>	435	91.1	6/23/95
	14	5,622,829	4/22/97	King <i>et al.</i>	435	6	4/19/95
	15	5,643,722	7/01/97	Rothschild <i>et al.</i>	435	6	5/11/94
	16	5,451,663	9/19/95	Kang <i>et al.</i>	530	367	4/08/93
	17	5,654,150	8/05/97	King <i>et al.</i>	435	6	6/07/95
	18	5,693,473	12/02/97	Shattuck-Eidens <i>et al.</i>	435	6	6/07/95
	19	5,709,998	1/20/98	Kinzler <i>et al.</i>	435	6	12/15/93
	20	5,760,207	6/02/98	Kinzler <i>et al.</i>	536	24.3	6/03/96
	21	5,783,397	7/21/98	Hughes <i>et al.</i>	435	7.1	6/12/96
	22	5,861,494	1/19/99	Soppet <i>et al.</i>	536	23.1	6/06/95
	23	5,879,890	3/09/99	Laken <i>et al.</i>	435	6	1/31/97

## FOREIGN PATENTS OR PUBLISHED FOREIGN PATENT APPLICATIONS

		Document Number	Publication Date	Country / Patent Office	Class	Subclass	Translation	
							Yes	No
	24	EP 0 234 799	02.09.87	EPO	C 12 P 21/02			
	25	WO90/05785	5/31/90	PCT				

## OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

26	Allen <i>et al.</i> , <i>Gel Electrophoresis and Isoelectric Focusing of Proteins</i> , Walter de Gruyter, New York 1984, pp. 17-62
27	<i>Antibodies: A Laboratory Manual</i> (E. Harlow and D. Lane, editors, Cold Spring Harbor Laboratory Press, 1988, pp. 53,72-73)
28	Bain <i>et al.</i> , "Site-Specific Incorporation of Nonnatural Residues during In Vitro Protein Biosynthesis with Semisynthetic Aminoacyl-tRNAs," <i>Biochemistry</i> 30:5411-21 (1991)

Examiner:

Date Considered:

EXAMINER:

Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449 (Modified)		U.S. Department of Commerce Patent and Trademark Office		Attorney Docket No.: AMBER-08501	Serial No.: 10/719,523
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (Use Several Sheets If Necessary) (37 CFR § 1.98(b))				Applicant: Kenneth J. Rothschild <i>et al.</i>	
				Filing Date: 11/21/03.	Group Art Unit: 1636
OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)					
	29	Bain <i>et al.</i> , "Site-Specific Incorporation of Non-Natural Residues into Peptides: Effect of Residue Structure on Suppression and Translation Efficiencies," <i>Tetrahedron</i> 47:2389-2400 (1991)			
	30	Bruce and Uhlenbeck, "Specific Interaction of Anticodon Loop Residues with Yeast Phenylalanyl-tRNA Synthetase," <i>Biochemistry</i> 21:3921-3926 (1982)			
	31	Crowley <i>et al.</i> , "The signal sequence moves through a ribosomal tunnel into a noncytoplasmic aqueous environment at the ER membrane early in translocation," <i>Cell</i> 73:1101-1115 (1993)			
	32	<i>Current Protocols in Molecular Biology</i> (F.M. Ausubel <i>et al.</i> editors, Wiley Interscience, 1993), pp. 10-16, 10-77			
	33	Czworkowski <i>et al.</i> , "Fluorescence Study of the Topology of Messenger RNA Bound to the 30S Ribosomal Subunit of <i>Escherichia coli</i> ," <i>Biochemistry</i> 30:4821-4830 (1991)			
	34	Da Poian, A. T., <i>et al.</i> , "Kinetics of intracellular viral disassembly and processing probed by Bodipy fluorescence dequenching," <i>J Virol Methods</i> 70(1), 45-58 (1998)			
	35	Doty <i>et al.</i> , "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Physical Chemicals Studies," <i>Proc. Natl. Acad. Sci. USA</i> 46:461-476 (1960)			
	36	DiCesare <i>et al.</i> , "A High-Sensitivity Electrochemiluminescence-Based Detection System for Automated PCR Product Quantitation," <i>BioTechniques</i> 15:152-59 (1993)			
	37	Felgner <i>et al.</i> , "Lipofection: A highly efficient, lipid-mediated DNA-transfection procedure," <i>Proc. Natl. Acad. Sci. USA</i> 84:7413-17 (1987)			
	38	Happ <i>et al.</i> , "New Approach to the Synthesis of 2'(3')-O-Aminoacyl Oligoribonucleotides," <i>J. Org. Chem.</i> 52:5387-91 (1987)			
	39	Hardesty <i>et al.</i> , "Extension and Folding of Nascent Peptides on Ribosomes." <i>The Translational Apparatus</i> , Nierhaus <i>et al.</i> ed: New York and London; Plenum Press. p. 347-358 (1993)			
	40	Hardesty <i>et al.</i> , "Ribosome function determined by fluorescence," <i>Biochimie</i> 74:391-401 (1992)			
	41	Heckler <i>et al.</i> , "Preparation of 2'(3')-O-Acyl-pCpA Derivatives as Substrates for T4 RNA Ligase-Mediated "Chemical Aminoacylation"," <i>Tetrahedron</i> 40:87-94 (1984)			
	42	Heckler <i>et al.</i> , "T4 RNA Ligase Mediated Preparation of Novel "Chemically Misacylated" tRNA <sup>Phe</sup> s," <i>Biochemistry</i> 23:1468-73 (1984)			
	43	Hemmila, I.A., <i>Chemical Analysis "Applications of Fluorescence in Immunoassays"</i> , (Wiley&Sons 1991) pp.138-159			
	44	Hudson, "Methodological Implications of Simultaneous Solid-Phases Peptide Synthesis. 1. Comparison of Different Coupling Procedures," <i>J. Org. Chem.</i> 53:617-624 (1988)			
	45	Johnson <i>et al.</i> , "Protein Synthesis and Secretion as seen by the Nascent Protein Chain," <i>The Translational Apparatus</i> , Nierhaus <i>et al.</i> ed: New York and London; Plenum Press. p. 359-370 (1993)			
	46	Johnson <i>et al.</i> , "N-Acetyllysine Transfer Ribonucleic Acid: A Biologically Active Analogue of Aminoacyl Transfer Ribonucleic Acids," <i>Biochemistry</i> 15:569-575 (1976)			
	47	Johnson, "Chemically Modified Aminoacyl-tRNA as a Probe of Ribosome Structure: the Synthesis and in vitro Activity of ε-N-acetyl-Lys-tRNA," 1973 Thesis Excerpts, University of Oregon, Eugene, Oregon			
	48	Karolin <i>et al.</i> , "Fluorescence and Absorption Spectroscopic Properties of Dipyrrometheneboron Difluoride (BODIPY) Derivatives in Liquids, Lipid Membranes, and Proteins," <i>J. Am. Chem. Soc.</i> 116:7801-7806 (1994)			
	49	Keller, R. C., <i>et al.</i> , "Characterization of the Resonance Energy Transfer Couple Coumarin-Bodipy and its Possible Applications in Protein-Lipid Research," <i>Biochem Biophys Res Commun</i> 207(2), 508-14 (1995)			
	50	Kim, D., and Choi, C., "A Semicontinuous Prokaryotic Coupled Transcription/Translation System Using a Dialysis Membrane," <i>Biotechnol Prog</i> 12, 645-649 (1996)			
	51	Kopp <i>et al.</i> , "Chemical Amplification: Continuous Flow PCR on a Chip," <i>Science</i> 280:1046 (1998)			
	52	Kozak, "Point Mutations Define a Sequence Flanking the AUG Initiator Codon that Modulates Translation by Eukaryotic Ribosomes," <i>Cell</i> 44:283-292 (1986)			
	53	Kramer <i>et al.</i> , "In Vitro engineering using synthtic tRNAs with altered anticodons including four-nucleotide anticodons," <i>Methods Mol Biol.</i> 77:105-16 (1998)			
	54	Kramer <i>et al.</i> , "N-terminal and C-terminal modifications affect of in vitro synthesized proteins," <i>Int J Biochem Cell Biol.</i> 31:231-41 (1999)			
	55	Krieg <i>et al.</i> , "Photocrosslinking of the signal sequence of nascent preprolactin to the 54-kilodalton polypeptide of the signal recognition particle," <i>Proc. Natl. Acad. Sci. USA</i> 83:8604-08 (1986)			
	56	Kudlicki, W. <i>et al.</i> , "Chaperone-dependent Folding and Activation of Ribosome-bound Nascent Rhodanse," <i>J Mol Biol</i> 244(3), 319-31 (1994)			
	57	Laemmli, U. K., "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophage T4," <i>Nature</i> 227:680-685 (1970)			
Examiner:			Date Considered:		
<b>EXAMINER:</b> Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.					

FORM PTO-1449 (Modified)		U.S. Department of Commerce Patent and Trademark Office		Attorney Docket No.: AMBER-08501	Serial No.: 10/719,523
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (Use Several Sheets If Necessary)				Applicant: Kenneth J. Rothschild <i>et al.</i>	
(37 CFR § 1.98(b))				Filing Date: 11/21/03	Group Art Unit: 1636
OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)					
58	Ma <i>et al.</i> , "In Vitro Protein Engineering Using Synthetic tRNA <sup>Ala</sup> with Different Anticodons," <i>Biochemistry</i> 32:7939-7945 (1993)				
59	Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic Acids: Biological Studies," <i>Proc. Natl. Acad. Sci. USA</i> 46:453-461 (1960)				
60	<i>Molecular Cell Biology</i> (J. Darnell <i>et al.</i> editors, Scientific American Books, N.Y., N.Y. 1991) pp. 119-132				
61	Nemoto <i>et al.</i> , "Fluorescence labeling of the C-terminus of proteins with a puromycin analogue in cell-free translation systems," <i>FEBS Letters</i> . 462:43-46 (1999)				
62	Neu and Heppel, "Nucleotide Sequence Analysis of Polyribonucleotides by Means of Periodate Oxidation Followed by Cleavage with an Amine," <i>J. Biol. Chem.</i> 239:2927-34 (1964)				
63	Noren <i>et al.</i> , "A General Method for Site-Specific Incorporation of Unnatural Amino Acids into Proteins," <i>Science</i> 244:182-188 (1989)				
64	Odom, O. W, <i>et al.</i> , "In vitro engineering using acyl-derivatized tRNA," In <i>Protein synthesis: Methods and Protocols</i> , PP.93-103, (Humana Press, Totowa, NJ.)				
65	Odom <i>et al.</i> , "Movement of tRNA but Not the Nascent Peptide during Peptide Bond Formation on Ribosomes," <i>Biochemistry</i> 29:10734-10744 (1990)				
66	Patchornik <i>et al.</i> , "Photosensitive Protecting Groups," <i>J. Am. Chem. Soc.</i> 92:6333-35 (1970)				
67	Pavlopoulos, <i>et al.</i> , "Laser action from a tetramethylpyromethene-BF <sub>3</sub> .sub.2 complex," <i>APP. OPTICS</i> 27:4998-4999 (1988)				
68	Picking <i>et al.</i> , "The use of synthetic tRNA as probes for examing nascent peptides on <i>Escherichia coli</i> ribosomes," <i>Biochimie</i> 73:1101-1107 (1991)				
69	Picking <i>et al.</i> , "Evidence for RNA in the Peptidyl Transferase Center of <i>Escherichia coli</i> Ribosomes as Indicated by Fluorescence," <i>Biochemistry</i> 31:12565-12570 (1992)				
70	Picking <i>et al.</i> , "The Conformation of Nascent Polylysine and Polyphenylalanine Peptides on Ribosomes," <i>J. of Biological Chemistry</i> 266:1534-1542 (1991)				
71	Picking <i>et al.</i> , "Fluorescence Characterization of the Environment Encountered by Nascent Polyalanine and Polyserine as They Exit <i>Escherichia coli</i> Ribosomes during Translation," <i>Biochemistry</i> 31:2368-2375 (1992)				
72	Picking <i>et al.</i> , "A synthetic alanyl-initiator tRNA with initiator tRNA properties as determined by fluorescence measurements: Comparison to a synthetic alanyl-elongator tRNA," <i>Nucleic Acids Research</i> 19:5749-5754 (1991)				
73	Pillai, "Photoremovable Protecting Groups in Organic Synthesis," <i>Synthesis</i> 1-26 (1980)				
74	Powell <i>et al.</i> , "Molecular Diagnosis of Familial Adenomatous Polyposis," <i>N. Engl. J. Med.</i> 329:1982-87 (1993)				
75	Pratt, "Coupled Transcription-Translation in Prokaryotic Cell-Free System," ( <i>Transcription and Translation</i> , B.D. Hames and S.J. Higgins, Editors, p. 179-209, IRL Press, Oxford, 1984)				
76	Promega Technical Bulletin No. 182; tRNA <sup>nascent</sup> TM: Non-radioactive Translation Detection System, Sept. 1993				
77	Reis, R. C., <i>et al.</i> , "A novel methodology for the investigation of intracellular proteolytic processing in intact cells," <i>Eur J Cell Biol</i> 75(2), 192-7 (1998)				
78	Rowan and Bodmer, "Introduction of a <i>myc</i> Reporter Tag to Improve the Quality of Mutation Detection Using the Protein Truncation Test," <i>Human Mutation</i> 9:172-176 (1997)				
79	Sampson and Uhlenbeck, "Biochemical and physical characterization of an unmodified yeast phenylalanine transfer RNA transcribed <i>in vitro</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 85:1033-37 (1988)				
80	Seong and RajBhandary, "Escherichia coli formylmethionine tRNA: Mutations in <sup>GGG</sup> sequence conserved in anticodon stem of initiator tRNAs affect initiation of protein synthesis and conformation of anticodon loop," <i>Proc. Natl. Acad. Sci. USA</i> 84:334-338 (1987)				
81	Shore <i>et al.</i> , "A Fluorescent Probe Capable of Incorporation into Nascent Polypeptide Chains," 1986 <i>Federation Proceedings</i> 45, 1566 Abstract				
82	Shore <i>et al.</i> , "Accessibility of AA-tRNA and Nascent Chain During Protein Synthesis," 1988 <i>FASEB Journal</i> 2, A1045 Abstract				
83	Shore, "The Use of Fluorescent-Labeled Amino Acids to Examine the Environment of Ribosome-Bound Nascent Polypeptide Chains," 1991 Dissertation, University of Oklahoma, Norman Oklahoma				
84	Spirin <i>et al.</i> , "A Continuous Cell-Free Translation System Capable of Producing Polypeptides in High Yield," <i>Sci.</i> 242:1162-64 (1988)				
85	Stephens, "High-Resolution Preparative SDS-Polyacrylamide Gel Electrophoresis: Fluorescent Visualization and Electrophoretic Elution-Concentration of Protein Bands," <i>Anal. Biochem.</i> 65:369-79 (1975)				
86	Treibs & Kreuzer, "Difluoroboryl-komplexe von di- und tripyrrylmethenen," <i>Liebigs Ann. Chem.</i> 718:208-223 (1968)				
Examiner:				Date Considered:	
EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.					

FORM PTO-1449  
(Modified)U.S. Department of Commerce  
Patent and Trademark Office

Attorney Docket No.: AMBER-08501

Serial No.: 10/719,523

**INFORMATION DISCLOSURE STATEMENT BY APPLICANT**  
(Use Several Sheets If Necessary)

(37 CFR § 1.98(b))

Applicant: Kenneth J. Rothschild *et al.*

Filing Date: 11/21/03

Group Art Unit: 1636

**OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)**

87	Tsalkova <i>et al.</i> , "The effect of a hydrophobic N-terminal probe on translational pausing of chloramphenicol acetyl transferase and rhodanese," <i>J Mol Biol.</i> 286:71-81 (1999)
88	Turcatti <i>et al.</i> , "Probing the Structure and Function of the Tachykinin Neurokinin-2 Receptor through Biosynthetic Incorporation of Fluorescent Amino Acids at Specific Sites," <i>J Biol Chem</i> 271(33), 19991-8 (1996)
89	Varshney U, RajBhandary UL, "Initiation of protein synthesis from a termination codon," <i>Proc Natl Acad Sci U S A</i> 87(4):1586-90 (1990)
90	Varshney <i>et al.</i> , "Direct Analysis of Aminoacylation Levels of tRNA <sup>a</sup> in Vivo," <i>J. Biol. Chem.</i> 266: 24712-24718 (1991)
91	Vecesey-Semjen <i>et al.</i> , "The Staphylococcal $\alpha$ -Toxin Pore Has a Flexible Conformation," <i>Biochemistry</i> 38 4296-4302 (1999)
92	Walker, B. <i>et al.</i> , "Functional Expression of the $\alpha$ -Hemolysin of Staphylococcus aureus in Intact Escherichia coli and in Cell Lysates," <i>J. Biol. Chem.</i> 267:10902-10909 (1992)
93	Yao S <i>et al.</i> , "SDS capillary gel electrophoresis of proteins in microfabricated channels," <i>PNAS</i> 96:5372-5377 (1999)
94	
95	
96	
97	
98	
99	
100	
101	
102	
103	
104	
105	
106	
107	
108	
109	
110	
111	

Examiner:

Date Considered:

**EXAMINER:**

Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record.**

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☒ **GRAY SCALE DOCUMENTS**
- ☐ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**